CLINICAL RESEARCH BASICS

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NIH Mission

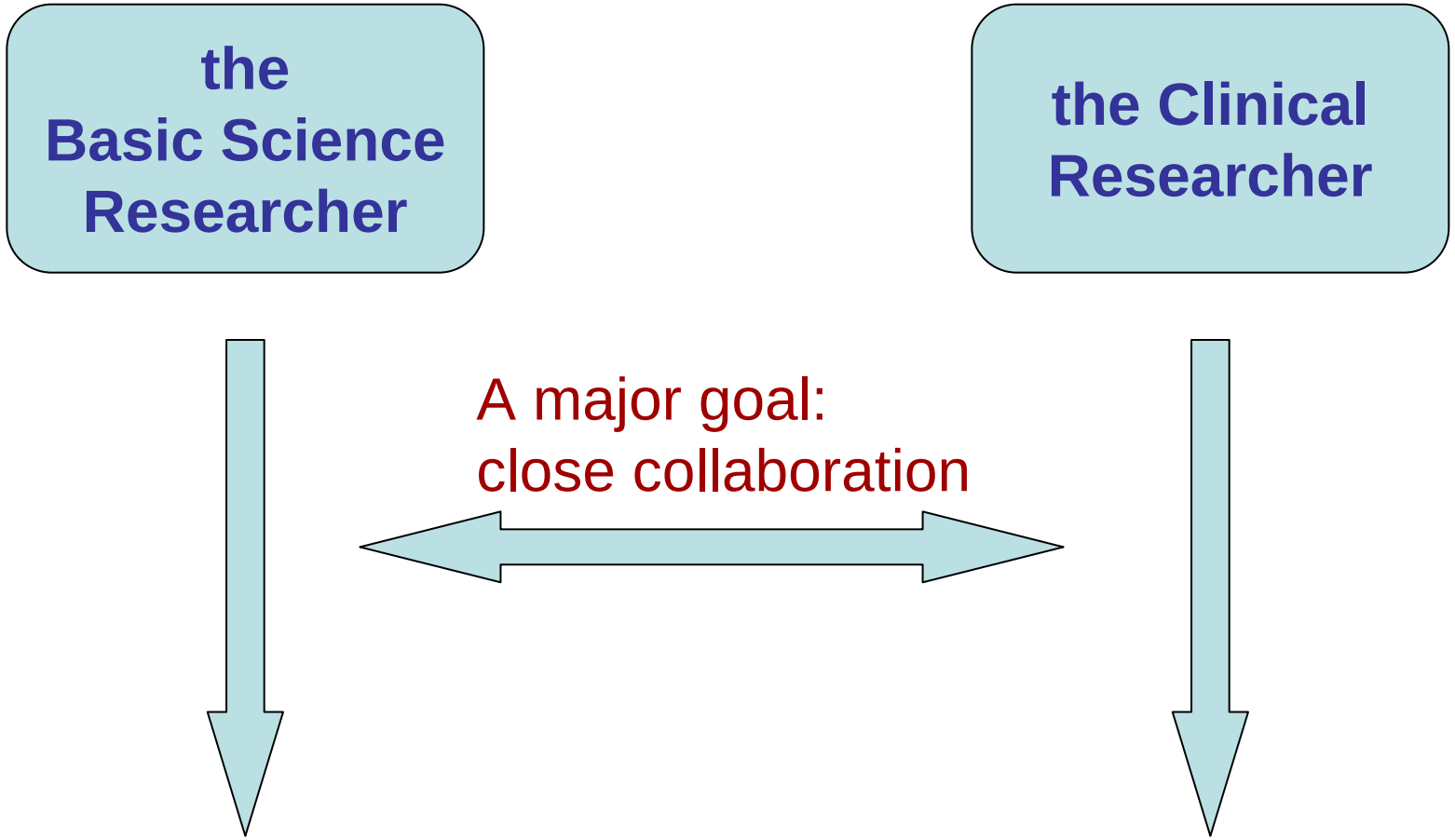
NIH is the steward of medical and behavioral research for the Nation.

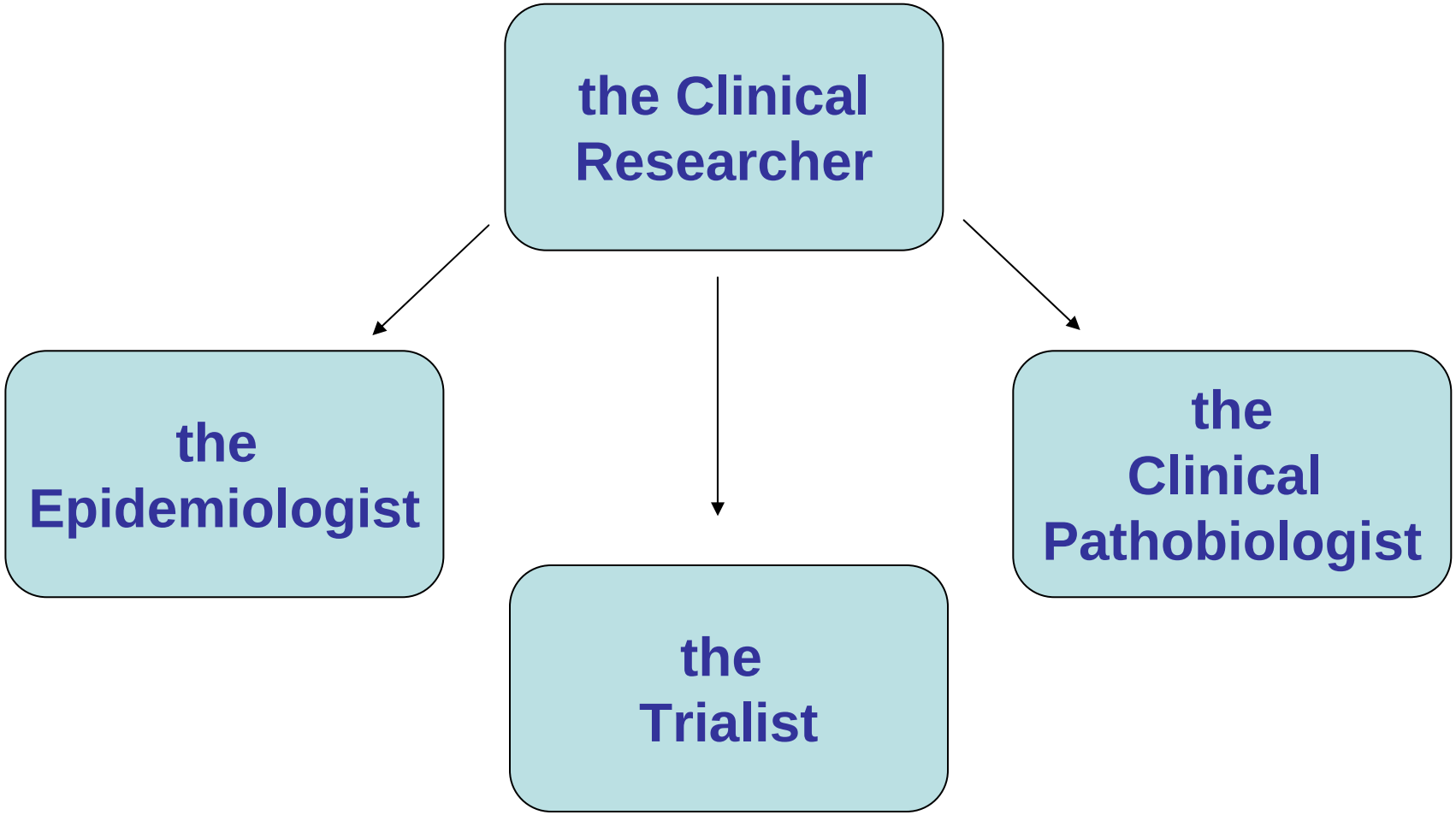
Its mission is **science in pursuit of fundamental knowledge** about the nature and behavior of living systems

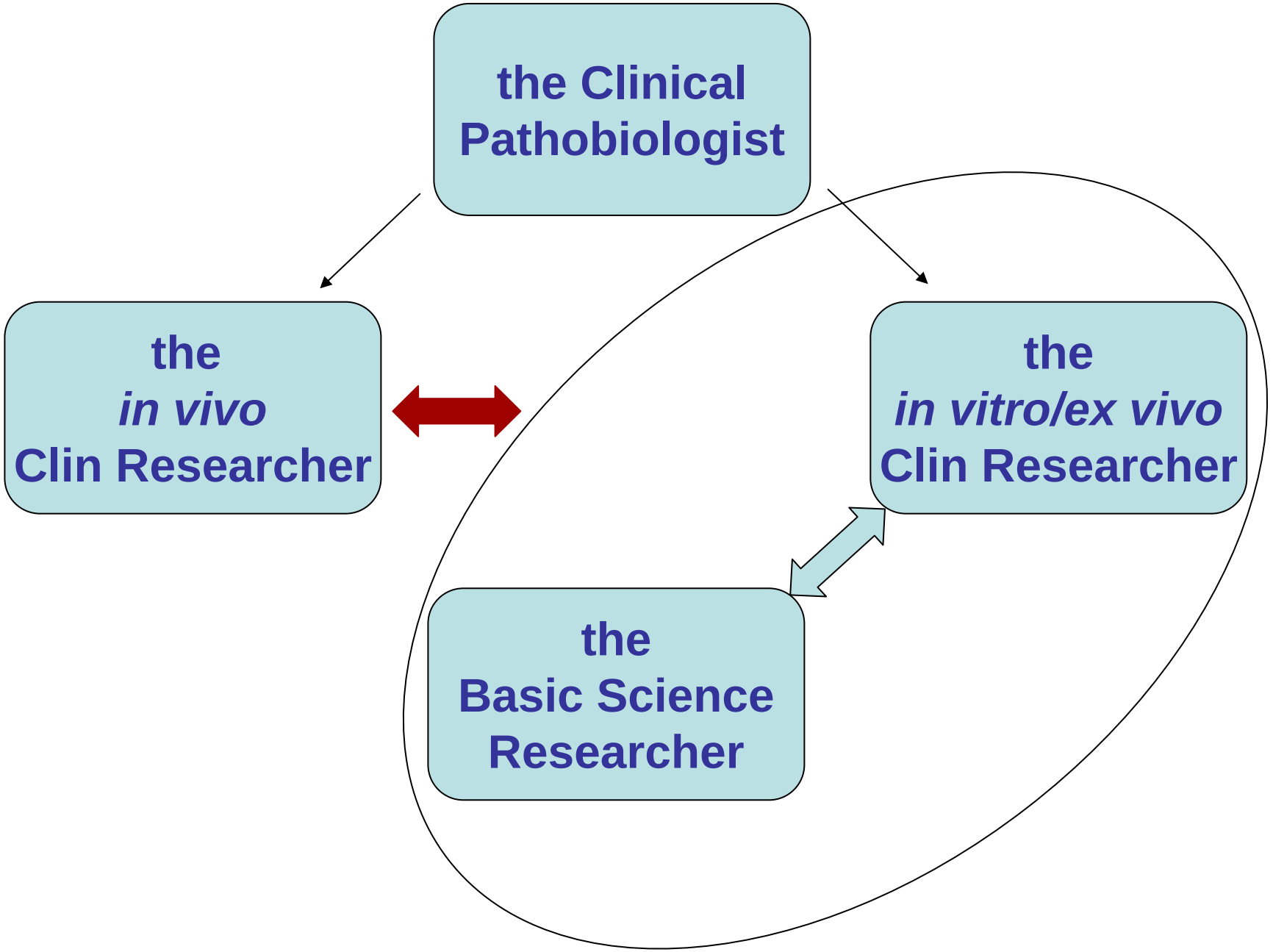
and

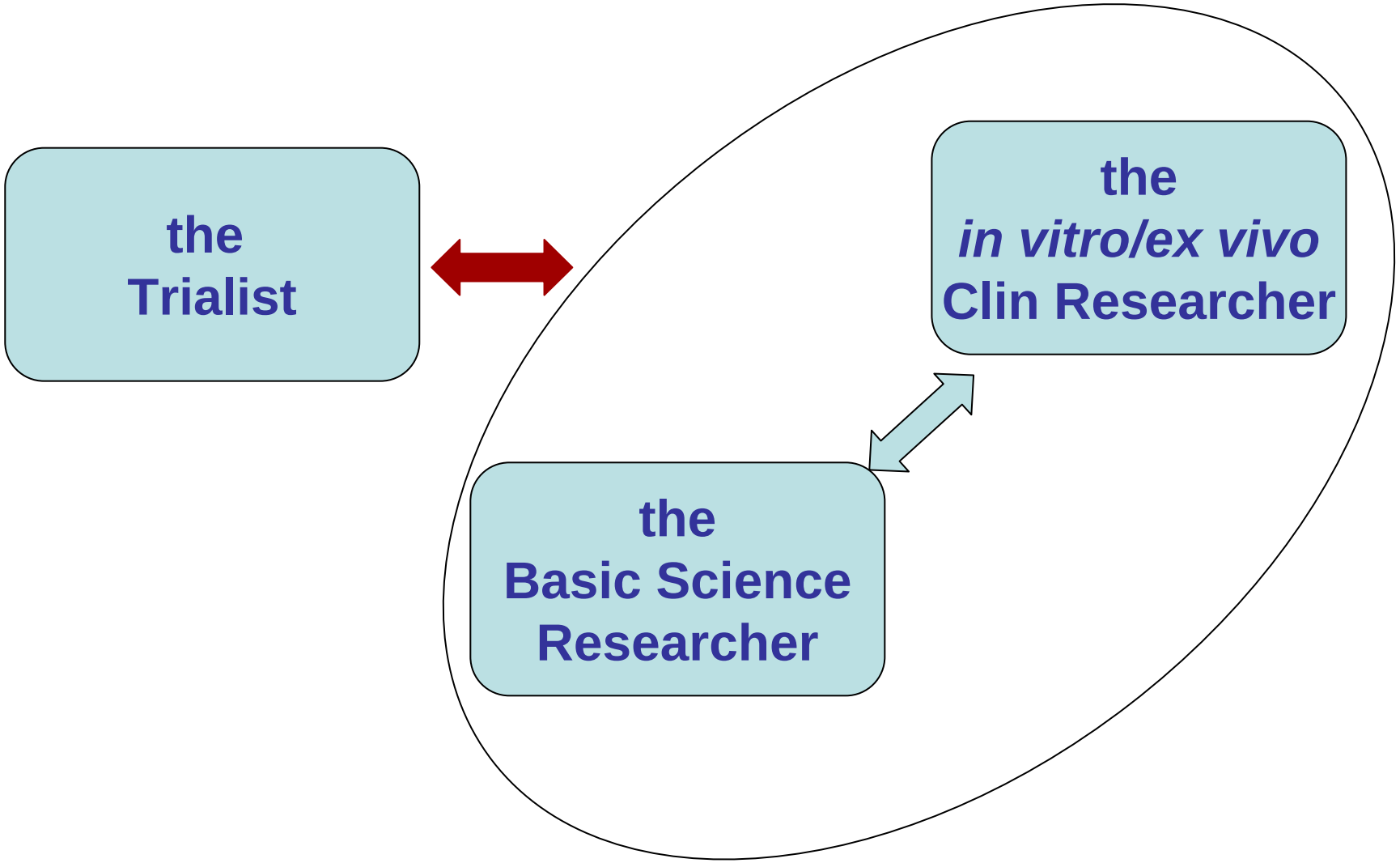
the **application of that knowledge to extend healthy life and reduce the burdens of illness and disability**.

Basic and Clinical Research




the Clinical Researcher
the Epidemiologist
the Trialist
the Clinical Pathobiologist

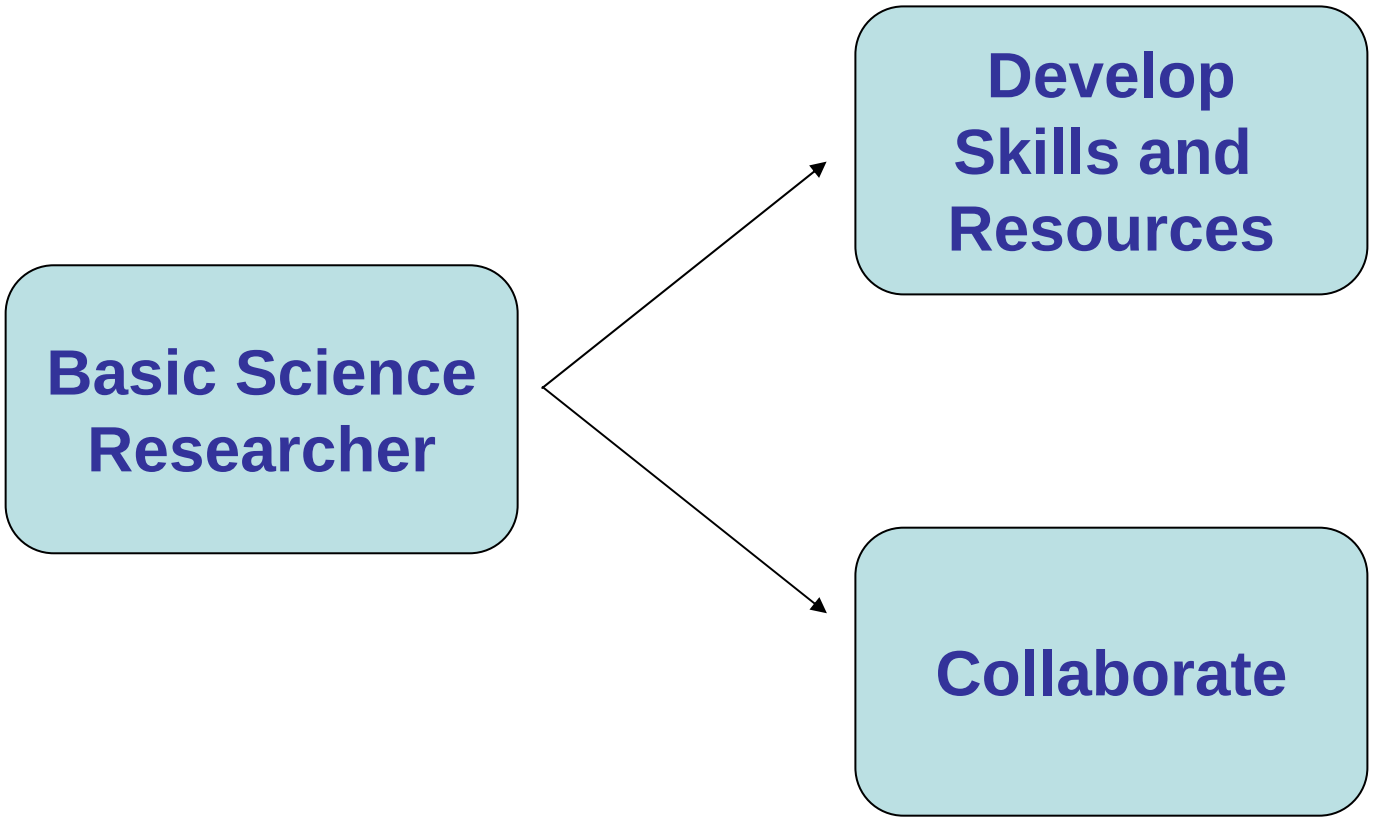

the Clinical Pathobiologist
the *in vivo* Clin Researcher
the *in vitro/ex vivo* Clin Researcher
the Basic Science Researcher


the
Trialist
the
in vitro/ex vivo
Clin Researcher
the
Basic Science
Researcher

Basic and Clinical Research Collaboration

- Increase the impact of the science on health
- Improve the success rates of applications
  - Typical criticism:
    - Basic science: “relevance to human disease?”
    - Clinical research: “non-mechanistic”

Getting involved in Clinical Research



Getting involved in Clinical Research

- Human Subject Protection:
  - Formal training very helpful for the Basic Science Researcher

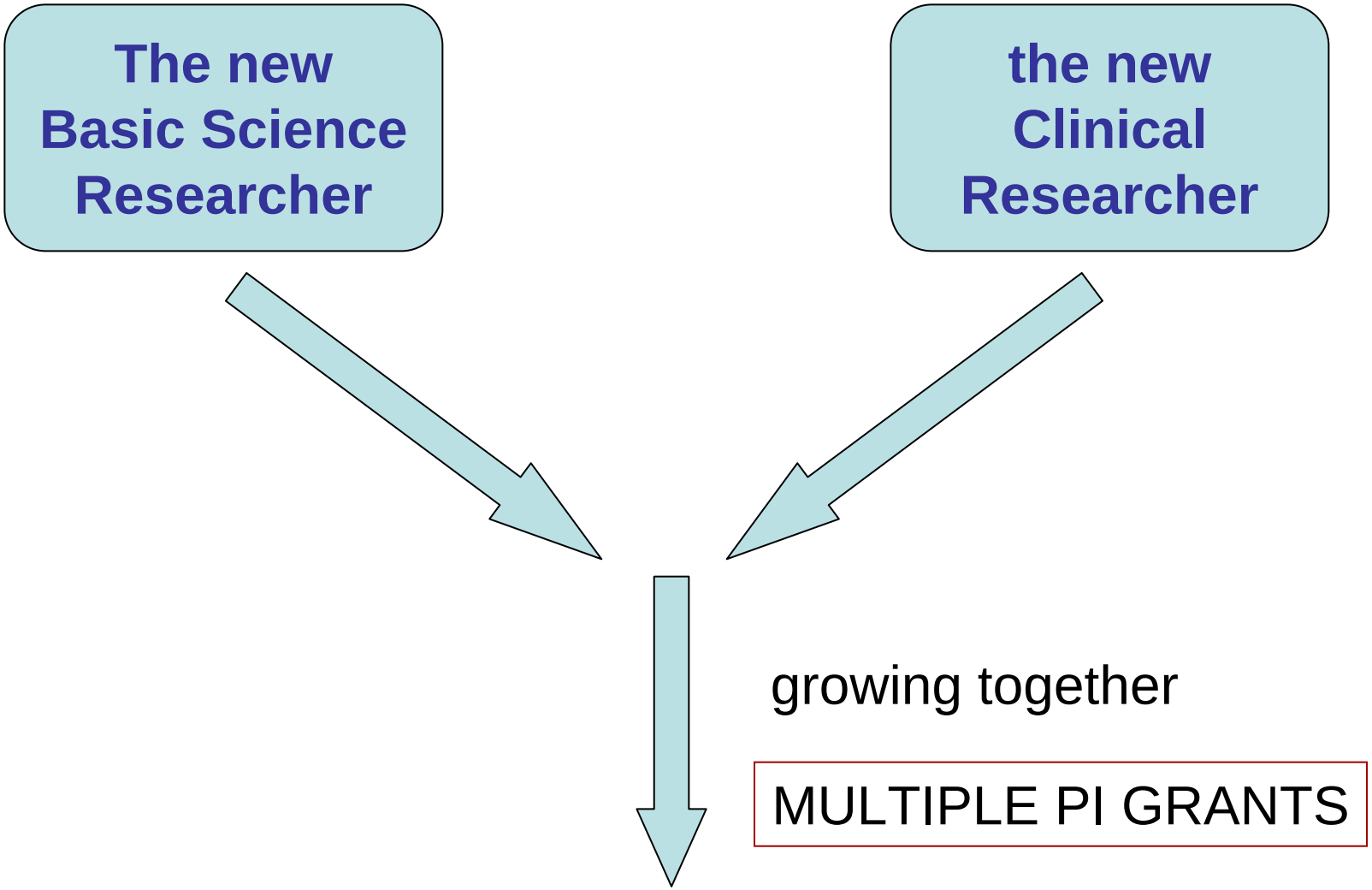
Getting involved in Clinical Research - Networking

- Disseminate your expertise and ideas
- Learn what the clinical researchers are doing
  - Attend clinical seminars
  - Present your work to clinical audiences
  - Organize small “think tanks” to include clinical researchers
  - Participate in professional societies with dual emphasis (research and clinical)
  - Write a review together with a clinician

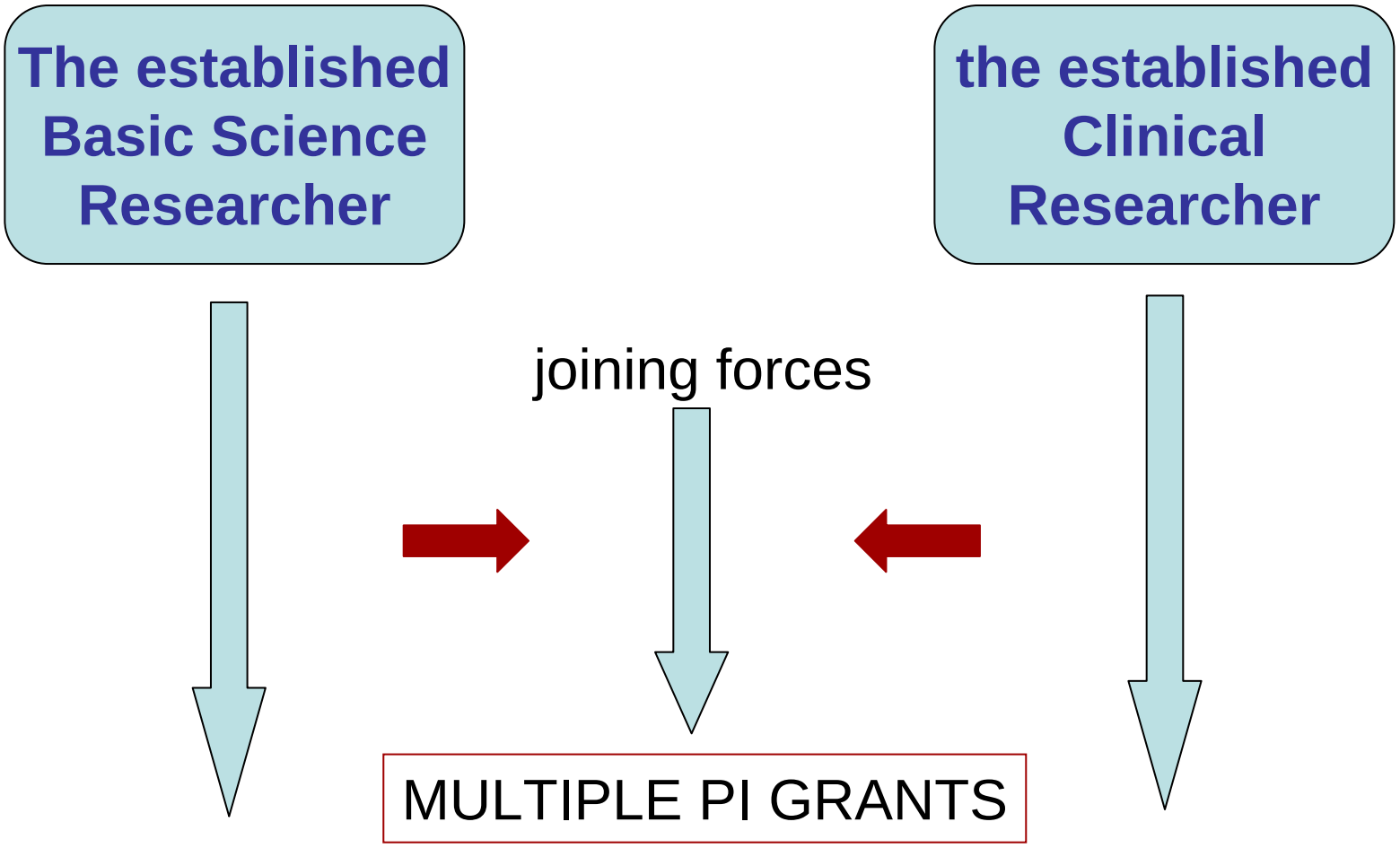
Getting involved in Clinical Research – Develop Collaborations

- Clinical Research Collaborators
  - Established: research agenda in place - more experience with regulatory aspects
  - New Investigators: more open to collaboration - more to gain - less experience with regulatory aspects
- Complementarity

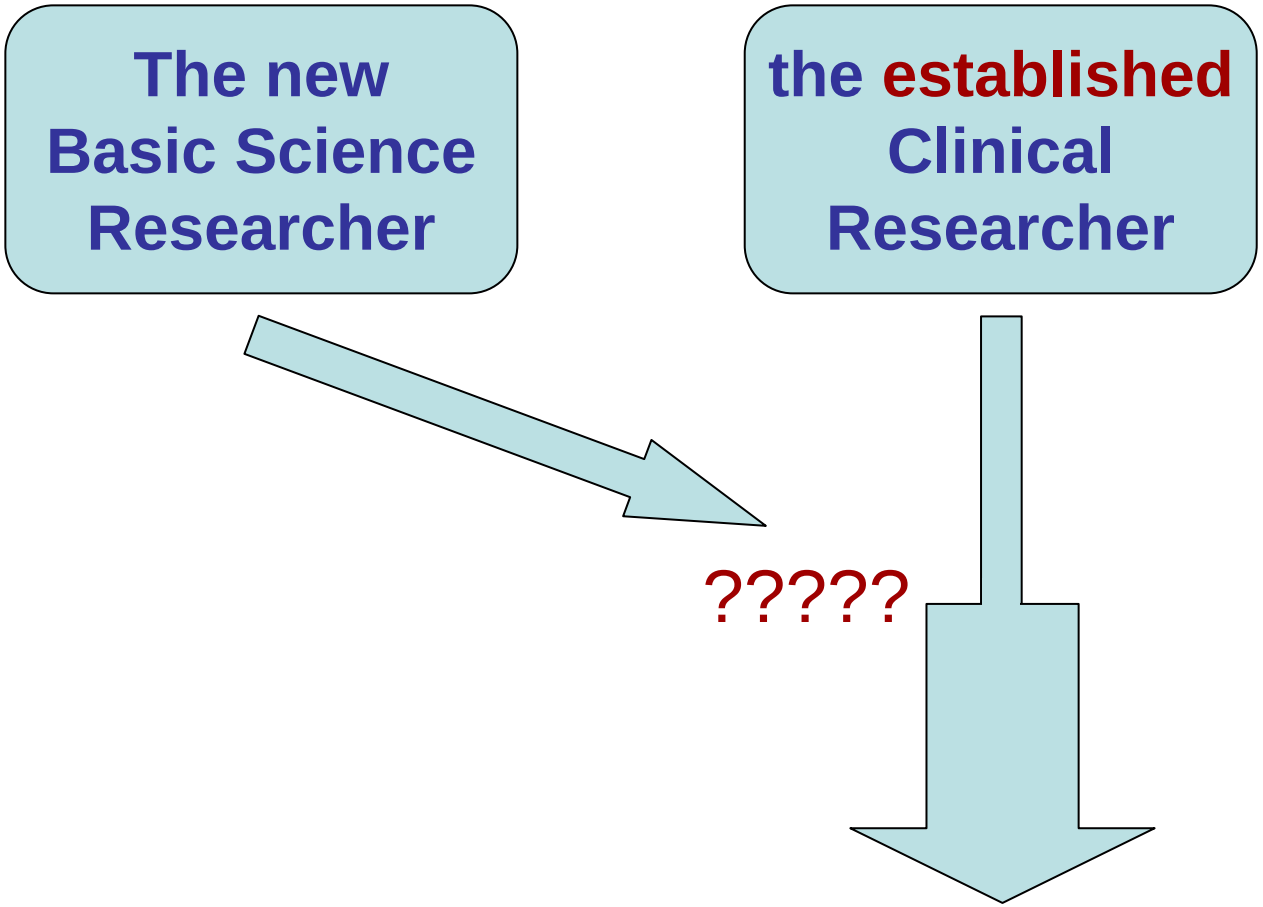
Develop Collaborations



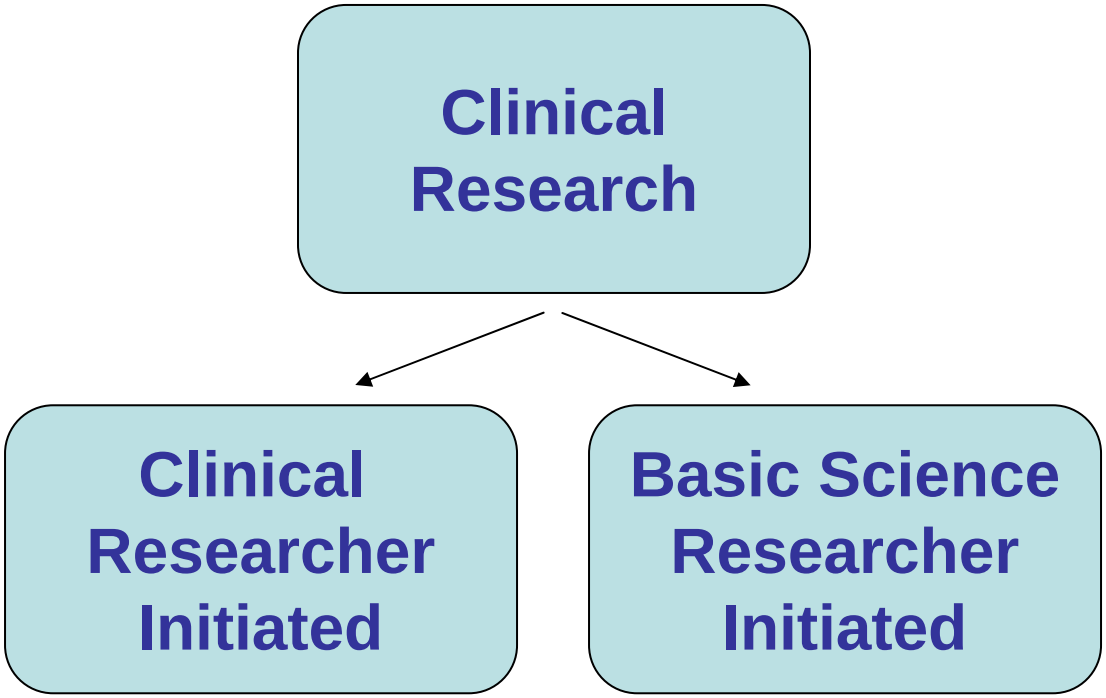
Develop Collaborations



Develop Collaborations



Getting involved in Clinical Research



“observational” vs. “mechanistic” flavor

A Clinical Researcher-Initiated Clinical Study

- The hypothesis: viral respiratory infections are more severe in people with allergies
- An observational study:
  - One-year follow-up of adults with and without allergies to record the severity of viral respiratory infections
- The basic researcher's hypothesis: *Protein X* production and/or signaling is defective in the presence of allergy
  - Is the severity of infection related to the levels of *Protein X* in nasal secretions?

A Basic Science Researcher-Initiated Clinical Study

- Clinical study of same design:
  - Measure levels of *Protein X* in nasal secretions on-off viral respiratory infections in allergic individuals and controls
  - Obtain biopsies and conduct immunofluorescence for *Protein X* receptors and downstream signaling proteins
  - Obtain epithelium from the same subjects, culture *ex vivo*, expose to rhinovirus and to *Protein X*

The Clinical Trial

- The hypothesis: viral respiratory infections are more severe in people with allergies
- The study:
  - Nasal administration of rhinovirus 39 in adults with and without allergies to record the severity of viral respiratory infections

Clinical Trials

- A prospective study of human subjects designed to answer questions about biomedical or behavioral interventions, e.g., drugs, treatments, or devices or new ways of using known treatments to determine whether they are safe and effective

Key Requirements for Clinical Trials

- Protocol, Consent Forms and Case Report Forms to be developed in cooperation with the NIAID Team
- Protocol and Consent Forms to be reviewed/approved by NIAID Data Safety Monitoring Board and by NIAID Clinical Research Committee
- FDA needs to be contacted if protocol involves the use of unapproved “drugs” (IND?)

Key Requirements for Clinical Trials

- Protocol needs to incorporate:
  - Data and Safety Monitoring Plan
    - Independent monitoring
    - AE and SAE recording and reporting (IRB, NIAID, FDA)
- Depending on the potential risk of the intervention
    - Data and Safety Monitoring may be conducted by NIAID
    - IND may be held by NIAID

Program Officer

+

Medical Officer

+

Project Manager

+

Regulatory Officer

R34 – Clinical Trial Planning Grant

- Support Planning of Investigator-Initiated Phase I, II, III, and IV clinical trials
- One Trial Per Application
- Development of the Clinical Protocol, Consent form(s), Data Management Planning, IRB, DSMB, IND, etc.
- One Year
- Budget: $75,000 for Phase I, $150,000 for Phase II, III, or IV
- Pre-Approval from NIAID Is Required

R34 – Clinical Trial Planning Grant

- The product of the R34 will be an application for a clinical trial implementation (U01) cooperative agreement

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